MSN Life Sciences Private Limited

LS3 TSD Activities

MSN Life Sciences Pvt. Limited
Date: 05-03-2024

Capacity Enhancement or Release

MSN Life Sciences Private Limited

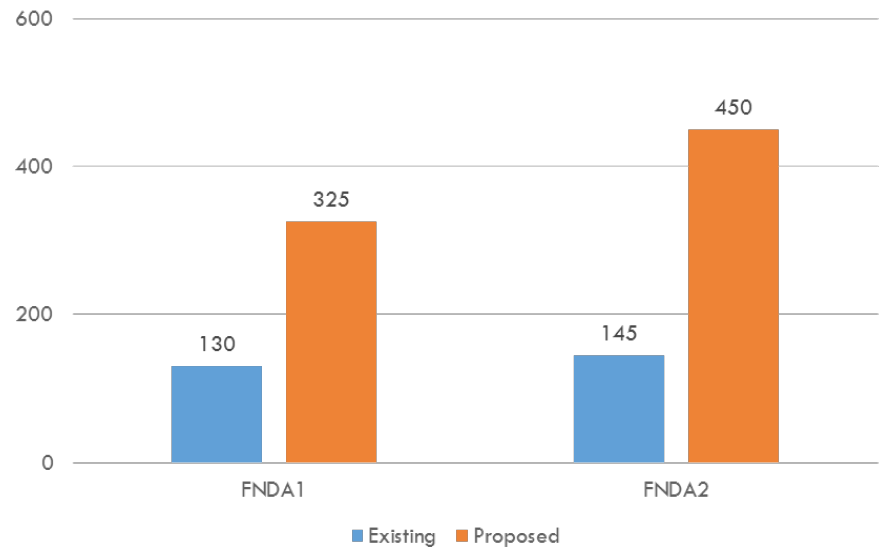
Product: Flecainide Acetate

FNDA1: Scale-up from 130 Kg to 325 Kg in existing B-Block facility,

FNDA2: Scale-up from 145 Kg to 450 Kg in existing F-Block Phase-IV.

Existing: 1.07 TPM. & **Proposed:** 4.30 TPM.

FNDA1		FNDA2	
Existing	Proposed	Existing	Proposed
130 Kg	325 Kg	145 Kg	370 Kg



Challenges:

1) Drying temperature @ 30±5°C, Acetic Acid Content spec narrow range (12.4-12.8% w/w) & Toluene removal (NMT 890 ppm)- **Dry Vacuum Pump Proposed.**

2) Coercer PSD requirement (D50- NLT 5 µm.)

Current Status:

Stage-1 (FNDA1)- Scale-up execution from 130 Kg to 325 Kg Completed in B-Block.

Stage-2 (FNDA2)- Currently Experimental batches with LS-3 R&D modified process at 250 Kg scale are u/process, further scale-up to be implemented.

Total Release of ~1795 KL Days (~60%)

Capacity Enhancement or Release

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Product:

Dabigatran Etexilate Intermediate

LDB1: 480 Kg to 640 Kg B.Size in I&C-Blocks.

LDA2: 500 Kg to 600 Kg B.Size in C-Block.

LDC1: 300 Kg to 500 Kg B.Size in C-Block.

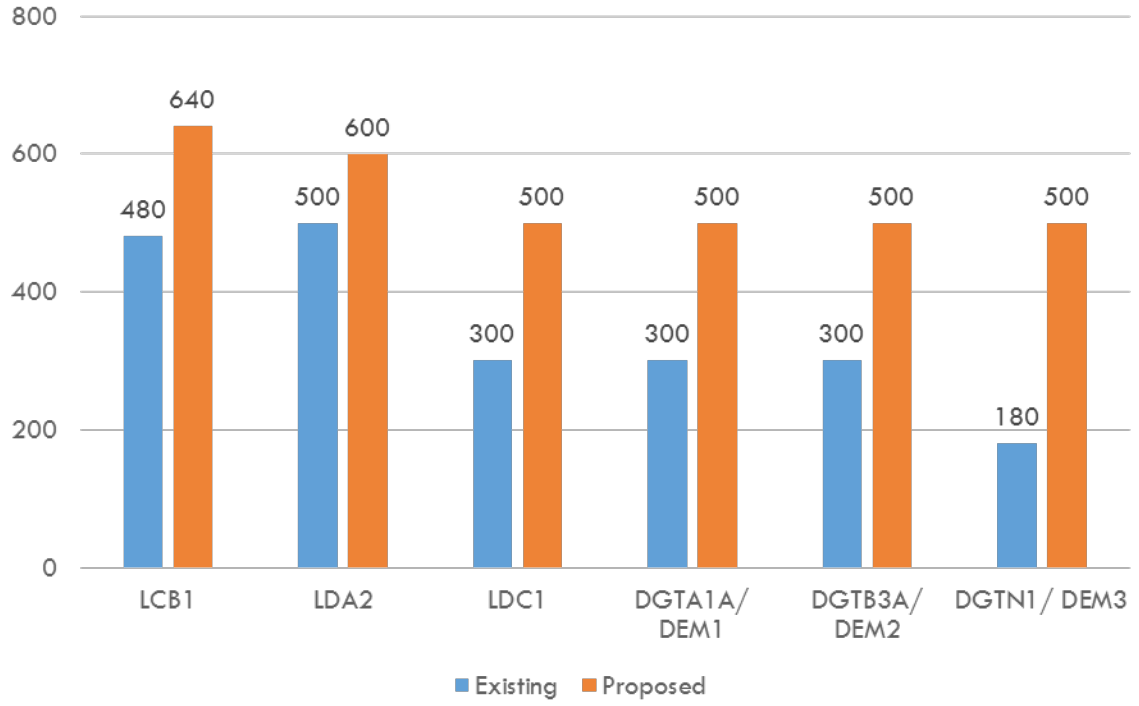
DGTA1A: 300 Kg in I-Block to 500 Kg B.Size in B-Block.

DGTB3A: 300 Kg to 500 Kg B.Size in C-Block.

DGTN1/ DEM3: 180 Kg in I&F-Blocks to 500 Kg B.Size in C-Block with additional Centrifuges installation for purifications.

Scale-up proposed to meet the monthly requirement of 5 TPM DEM3 & 14 TPM LDC1 material from LS3 Unit.

Stage	LDB1	LDA2	LDC1	DGTA1A/ DEM1	DGTB3A/ DEM2	DGTN1/ DEM3
Existing	480 Kg	500 Kg	300 Kg	300 Kg	300 Kg	180 Kg
Proposed	640 Kg	600 Kg	500 Kg	500 Kg	500 Kg	500 Kg



<u>Current Status:</u> LDB1, LDA2, LDC1, DGTA1A & DGTB3A stages scale-up Completed as per proposal. DEM3 currently 180 Kg scale batches are under process in I-Block & F-Block, 500 Kg scale-up to be planned in C-Block.

Capacity Enhancement or Release

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Product: Ranolazine

RLNA1: Scale-up from 500 Kg in A-Block to 900 Kg in C-Block,

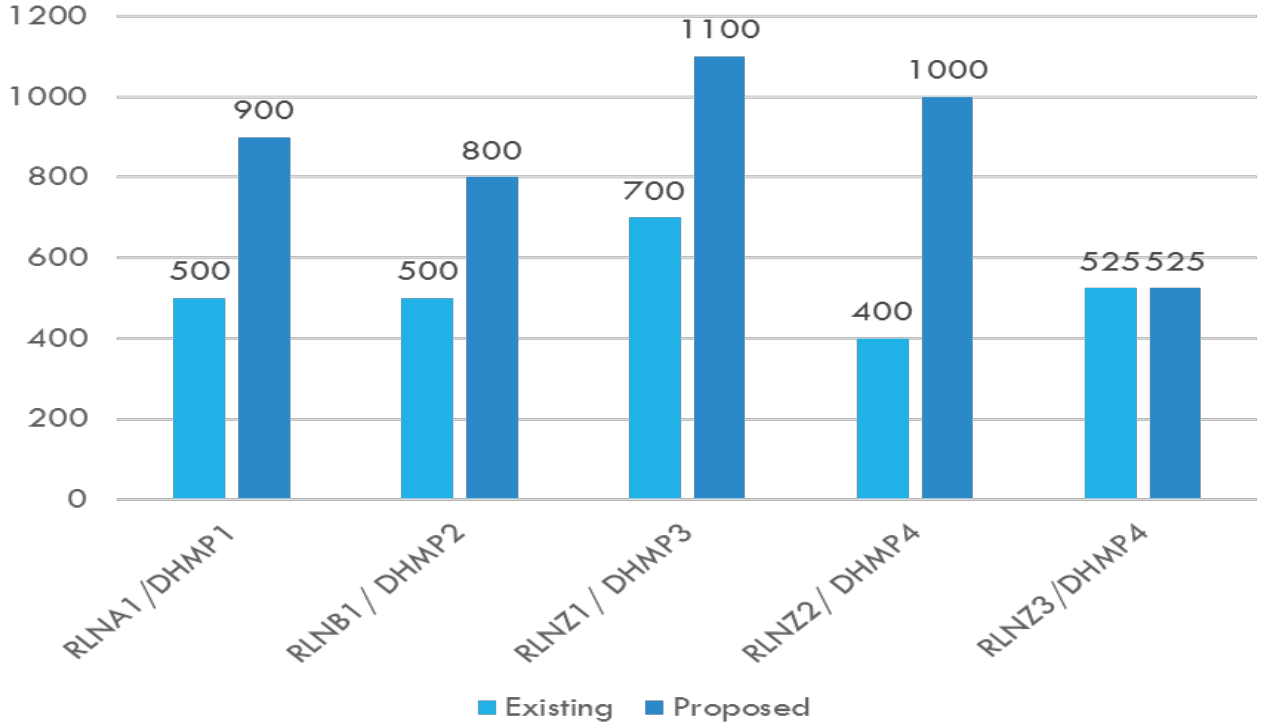
RLNB1: Scale-up from 500 Kg in A-Block to 800 Kg in C-Block.

RLNZ1: Scale-up from 700 Kg in B/A-Block to 1100 Kg in C-Block.

RLNZ2: Scale-up from 400 Kg in E/F-Block to 1000 Kg in C-Block.

RLNZ3: Additional cleanroom E-III along with existing F-IV with 525 Kg Batch Size.

RLNA1/ DHMP1		RLNB1/DHMP2		RLNZ1/DHMP3		RLNZ2/DHMP4 (Crude)		RLNZ3/DHMP4 (Pure)	
Existing	Proposed	Existing	Proposed	Existing	Proposed	Existing	Proposed	Existing	Proposed
500 Kg	900 Kg	500 Kg	800 Kg	700 Kg	1100 Kg	400 Kg	1000 Kg	525 Kg	525 Kg



Existing: 5.5 TPM.

Proposed: 17 TPM.

Current Status: RLNA1 Scale-up completed. Campaign stopped currently due to Dabigatran product. Remaining stages scale-up to be implemented in next campaign.

Total Release of ~9154 KL Days (~16%)

New Products at LS-III

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New Products Status at LS-III

S.#	Product	API Qty	Stage Code	Raw Materials		Tech Transfer	Facility Readyness	Document Approval	Execution					
				Received	Analysis				Trial	Validation-1	Validation-2	Validation-3	Commercial	Analysis
1	Mesalamine	700 Kg	MEAM1	Received	Completed	09-10-2023	Completed	Completed	Completed	Completed	Completed	Completed	NA	Completed
			MEAM2	Received	Completed	09-10-2023	Completed	Completed	Completed	Completed	Completed	Completed	Completed	Completed
			MEAM3	Received	Completed	09-10-2023	Completed	Completed	Completed	Completed	Completed	Completed	Pending	C1 Execution pending
2	Vonoprazan Fumarate	100 Kg	VFNA1	Received	Completed	28-09-2023	Completed	Completed	Completed	Completed	Completed	Completed	NA	
			VPNA1	Received	Completed	05-02-2024	Completed	Completed	U/ Analysis					
			VPNA2	Received	Pending	Pending								
			VPNA3	Received	Pending	Pending								
			VPNA4	Received	Pending	Pending								
3	Chlorthalidone	500 Kg	CRTA1	Received	Completed	18-01-2024	Completed	Completed	Completed	To be Started				
			CRTD1	Received	Completed	17-02-2024	Completed	Completed	U/ Analysis					
			CRTD2	Received	Pending	Pending								
			CRTD3	Received	Pending	Pending								
			CRTD4	Received	Pending	Pending								
4	Vericiguat	7 Kg	VRGT1	Received	Completed	Completed	Completed	Completed	Completed	U/Process				
			VRGT2	Received	Pending	Pending								
			VRGT3	Received	Pending	Pending								
			VRGT4	Received	Pending	Pending								

Trouble shooting

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PIN MILL Trials for Levetiracetam To Meet Desired PSD	
Product & Stage:	**Levetiracetam Pharma (LVTC2)**
Existing Situation	**Requirement**
Levetiracetam Pharma material is coarser and PSD is not meeting the requirement. ~5 to 6 times Milling operation is being performed in Multimill for Sieve Top materials to meet the required PSD.	Required PSD range & Regular Trend in validations is D90 ~165 Microns.
Proposal:	
1) As the required PSD (~165 microns) is less than the multi mill mesh size (i.e. 0.25 mm/ 250 microns), material is constantly passing through miller mesh and PSD is not meeting the requirement. 2) Pin Mill Trials were performed for Levetiracetam Sieve Top material to meet the desired PSD (D90 ~165 microns) and to avoid multiple milling operation (~5-7 times)	
Results & Way forward:	
Below are the Pin Mill trail results. With 3000 RPM, D10-20.3 microns, D50-81.2 microns & D90-187 microns With 3300 RPM, D10-17.6 microns, D50-70.5 microns & D90-164 microns. Pin mill material with 3300 RPM is meeting the requirement, to be implemented in regular commercial batch. Material loss can be avoided, Effective clean room utilization & manpower by implementing Pin Mill operation in place of multiple milling operations (5-7 times).	

Unwanted Salt Filtration Optimization in LDC1 Stage of Dabigatran

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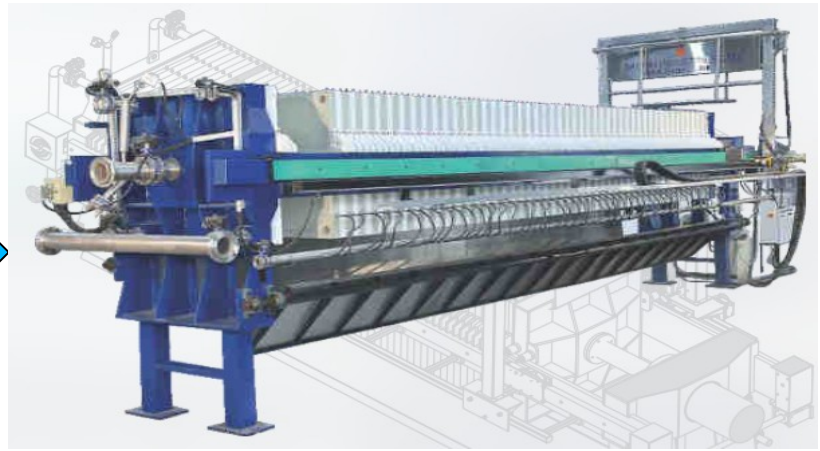

Challenges in Existing Open Nutsche Filter:

- Existing Filter Capacity- 1.0 KL x 2 Nos of Open Nutsche Filters.
- Rate of Filtration & filtration flux is slow (<20 LPM/m2) due to slimy nature of unwanted salt resulting in impact on productivity.
- Filtration in hot condition 45-50°C & Reaction mass is mixture of Water + Toluene resulting in potential fire hazard.

Advantages in Membrane Press Filter:

- Rate of Filtration & filtration flux will be more in proposed Filter Press.
- Process cycle time will be reduced due to more filtration area.
- Reduces the wash water consumption.

Current Status: PO released for Membrane Press Filter with 15 m2 area for I-Block, Trial to be taken after receiving the equipment to LS-III

Customer Support for PSD

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S.#	Block	Product	Activity	Status	Remarks
1	F-Block	Opicapone	2.0 Kg x 2 Nos Samples for ABBOTT with Below PSD Specifications. **Fine Material (2 Kg):** D(95): Not more than 10 µm D(50): Not more than 6 µm D(10): Not more than 4 µm **Coarser Material (2 Kg):** D(95): Not more than 70 µm D(50): Between 10-45 µm D(10): Not less than 4 µm	Existing Material PSD Trend is D(95) : 11-14 µm D(50) : 4-5 µm D(10) : 2-3 µm **Fine Material (2 Kg):** Micronized material with 0.6 ± 0.2 Kg/cm2 feed & chamber pressure is meeting the requirement, Dispatch completed. **Coarser Material (2 Kg):** Batch executed at Pilot plant with modified process & material dispatched with coarser specification.	
2	F-Block	Mesalamine	MSNF requirement for 6.0 Kg x 2 Nos with below PSD specifications. **Coarser Material (2 Kg):** D(90): 50-100 µm **Fine Material (2 Kg):** D(90): Below 10 µm	**Coarser Material (2 Kg):** Material with Additional Milling operation (0.5 mm mesh & full RPM) is meeting the specification. Material dispatched with D90- 82 µm **Fine Material (2 Kg):** Micronization trial with 6.5 ± 0.2 Kg/cm2 feed & chamber pressure is meeting the required specification. Analysis Under Process (D90- 6.8 µm) & Material	

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Thank you